

discharge, left ventricular ejection fraction (LVEF) was measured with a radionuclide technique.

Results: Results are shown in the Table. Data for pts with anterior MI in relation to LDH_{Q48} (mean ± SD) and LVEF (mean ± SD) are shown separately.

	TIMI 0 (65%)	TIMI 1 (10%)	TIMI 2 (12%)	TIMI 3 (13%)
MBG 2/3 (%)	75	81	89	96
LDH _{Q48} All MI	1513 ± 1264	1159 ± 1484	1014 ± 956	748 ± 700
Anterior MI	1816 ± 1404	1601 ± 2126	1115 ± 1064	808 ± 831
LVEF (%) All MI	43 ± 11	46 ± 11	44 ± 11	48 ± 11
Anterior MI	36 ± 10	39 ± 13	41 ± 11	46 ± 11

Conclusion: Not only TIMI 3 flow, but any increase in initial TIMI flow of the IRV is associated with a better preserved LVEF, smaller enzymatic infarct size and higher MBG. Further research, involving (pharmacological) treatment leading to improvement of initial patency of the IRV in pts with acute MI treated with PA, should be encouraged.

Noon

1001-5

Blood-Borne Hematopoietic Cells of Monocyte Origin: Precursors to Neointimal Myofibroblasts After Coronary Artery Injury

Robert S. Schwartz, Arturo G. Touchard, Antoni Bayes-Genis, Minnesota Cardiovascular Research Institute, Minneapolis, MN

Background The origin of neointimal myofibroblasts following coronary artery injury remains an intriguing, but unknown question. Since macrophages participate prominently in neointimal formation through early colonization of arterial lesion sites, we questioned the relationship between these cell lines. We thus studied whether monocyte/macrophage lineage cells contribute to neointimal cellular mass in a porcine model of thermal coronary artery injury, a method that severely depletes normal medial cells and grows thick neointimal hyperplasia by 28 days.

Methods and Results Thermal coronary artery injury using a radiofrequency-heated angioplasty balloon caused medial smooth muscle cell necrosis and transformation of the media into an acellular barrier. Neointimal hyperplasia developed at these injury sites and was evaluated by light microscopy, electron microscopy and immunohistochemistry. At day 3 after injury, blood monocytes adhered to the luminal side vessel wall only, and infiltrated the fibrotic media. At day 14, 42 ± 3.9% of neointimal cells had monocytic nuclear morphology and expressed macrophage-specific antigen SWC3 (identified by monoclonal antibody DH59B). Moreover, 9.2 ± 1.8% of neointimal cells co-expressed SWC3 and alpha-smooth muscle actin and had ultrastructural characteristics intermediate between macrophages and myofibroblasts. At day 28, 10.5 ± 3.5% of cells expressed SWC3 and 5.2 ± 1.8% of cells co-expressed SWC3 and alpha-smooth muscle actin.

Conclusions These data suggest that monocyte/macrophage lineage cells of hematopoietic origin abundantly populate the neointima. Myofibroblasts within neointimal hyperplasia may originate from these precursor cells, thus suggesting a blood-borne route of colonization.

Noon

1001-6

Tissue Engineered Endothelial Cells Inhibit Early Events in the Vascular Response to Injury to Prevent Restenosis

Sahil A. Parikh, Brad C. Carofino, Amy C. Lee, Adam Groothuis, Philip Seifert, Helen M. Nugent, Elazer R. Edelman, Brigham and Women's Hospital, Boston, MA, Massachusetts Institute of Technology, Cambridge, MA

Background: Perivascular implantation of tissue engineered endothelial cells (TEEC) after vascular injury profoundly inhibits neointimal hyperplasia (NIH). However, the time course and mechanism of this effect is unknown. NIH in the rat carotid balloon injury model occurs in a stereotypic stepwise progression. By developing genetically modified TEEC expressing a "suicide gene," we can control the time during which they exert their effect. These TEEC can help identify the critical time window when the implants exert their influence and may implicate their putative mechanism of action.

Methods: Bovine aortic endothelial cells (BAE) were transfected with the human herpes simplex virus thymidine kinase (TK) gene to render them sensitive to ganciclovir (GCV). BAE+TK were grown to confluence on Gelfoam and had the same growth kinetics and biologic potency as control cells but were sensitive to GCV at low concentrations. The BAE+/-TK were grown on Gelfoam and placed in the perivascular space around balloon injured rat carotid arteries. Rats randomly received BAE+TK, BAE-TK, or nothing (control) after balloon injury. GCV was administered early (day 1-7), late (day 5-11) or not at all. Rats were sacrificed and arteries examined histologically for NIH.

Results: Two weeks after injury, extensive NIH was observed in control animals with intima:media area ratios of (0.80±0.19). Early administration of GCV to BAE+TK constructs significantly abrogated TEEC inhibition of NIH (0.45±0.06). NIH was still effectively inhibited in animals with implants containing BAE-TK or BAE+TK that received GCV late (0.11±0.04 and 0.19±0.05). Immunohistochemistry demonstrated the lethal effect of GCV on BAE+TK.

Conclusions: The application of perivascular TEEC for only the first few days after injury had a significant inhibitory effect on NIH. This suggests that the mechanism of action of TEEC influences one of the early events in the vascular response to injury such as inflammation or smooth muscle cell proliferation. Moreover, the use of this technique to further elucidate biologic mechanisms will prove invaluable in the tissue engineering field.

1001-7

The Use of Abciximab During Percutaneous Coronary Angioplasty in Patients With Acute Coronary Syndrome Improves the Microcirculatory Function: Results of a Prospective Randomized Study

Piotr Kwiatkowski, Alessandro Manzoli, Costantino Caroselli, Fabrizio Imola, Alessandro Pappalardo, Eugenio Caradonna, Alessandro Boccanelli, Francesco Prati, Cath Lab San Giovanni Hospital, Rome, Italy

Background. The use of abiciximab during PTCA in patients with acute coronary syndrome (ACS) was found to improve the clinical outcome, probably due to improvement of post-PTCA microcirculatory function. This study was performed in patients with ACS to define whether abiciximab is capable to improve the post-PTCA microcirculation. **Methods.** We carried out a prospective randomized study including 136 patients with non ST elevation ACS and scheduled for PTCA of the target lesion. Sixty-eight patients received abiciximab (group 1) whilst 70 patients were not treated with any GP IIb/IIIa inhibitors (group 2). All cases underwent QCA, CTFC and quantitative myocardial blush (MBG) assessment, applying a software that evaluates the videointensity in a given region of interest and using a 1 to 6 points (poor-optimal) perfusion scale. **Results** Group1 and group 2 were comparable as regard incidence of diabetes (15% vs 18%), stenting (93% vs 89%), procedures in the LAD(44% vs 44%). CKMB increase above range value was found in a lower percentage of cases in the group with a 6 points MBG index in comparison with the group with MBG index ≤ 5 points, although the difference was non significant (3% vs 14% respectively; p=0.14). Pre- and post-PTCA %DS and CTFC were comparable, whilst a statistically lower value of MBG post-PTCA was found in Group1 (p= 0.02).

Conclusions This study shows that the administration of abiciximab improves the microcirculatory function in patients treated with angioplasty for acute coronary syndromes.

	QCA %DSo:p>	CTFC	MBG
--	-------------	------	-----

	Pre-PTCA	Post-PTCA	Pre-PTCA	Post-PTCA	Post-PTCA
Group 1	74.9 ± 15.3	17.5± 14.9	30.1 ± 18.7	18.9 ± 8.7	3.6 ± 2.0
Group 2	71.7 ± 12.9	17.2 ± 8.8	23.7 ± 11.3	20.2 ± 8.2	2.9 ± 2.0

Noon

1001-8

Long-Term Results of ISAR-REACT: A Randomized Trial Evaluating Abciximab in Patients With Elective Percutaneous Coronary Intervention After Pretreatment With a High Loading Dose of Clopidogrel

Helmut Schuhlen, Adnan Kastrati, Julinda Mehilli, Josef Dirschinger, Franz Dotzer, Jurrien ten Berg, Franz-Josef Neumann, Peter B. Berger, Albert Schomig, The ISAR-REACT Investigators, Deutsches Herzzentrum, Munich, Germany, 1. Med. Klinik rechts der Isar, Munich, Germany

Background: The standard antithrombotic regimen after stent placement comprises clopidogrel + aspirin. Clopidogrel however has a delayed onset of action which may be accelerated by a loading dose. In addition, glycoprotein IIb/IIIa inhibitors have been shown to reduce 30-day ischemic event rates. ISAR-REACT is a double blind, placebo-controlled multicenter randomized trial evaluating whether abciximab is beneficial in low and intermediate risk patients undergoing elective PCI after pretreatment with a high, 600 mg loading dose of clopidogrel at least 2 hours prior to PCI. Previous studies have indicated that a maximal antiplatelet effect of clopidogrel is achieved with this regimen within 2 hours. The primary endpoint (cumulative incidence of death, myocardial infarction, and urgent revascularization within 30 days) has been presented at the ACC 2003.

Methods: This analysis comprises prespecified secondary long-term endpoints, based on a 12-month clinical follow-up of all patients, and a subset of 1600 patients with planned repeat angiography after 6 months.

Results: The study enrolled 2159 patients undergoing PCI with stent placement between May 2000 and February 2003: 1079 were randomly assigned to abciximab, 1080 to placebo. All patients had received 600 mg clopidogrel >2 hours prior to PCI. As previously reported, the incidence of the primary endpoint at 30 days was 4.2% in the abciximab group, and 4.0% in the placebo group (p=0.82). No significant differences were seen for the rate of death, myocardial infarction, or bleeding complications. Profound thrombocytopenia occurred in 0.9% of the abiciximab group versus none in the placebo group (p=0.002). As enrolment ended in February 2003, clinical long-term follow-up and repeat angiography are still ongoing.

Conclusions: With respect to the primary endpoint, this study indicates that in low to intermediate risk patients undergoing elective PCI after pretreatment with 600 mg clopidogrel, the additional administration of abciximab is associated with no clinically measurable benefit within the first 30 days. Data on long-term 1-year clinical as well as 6-month angiographic follow-up will be presented.